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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/761,893	01/17/2001	Shih-Chieh Hung	11709-003001	6011

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EXAMINER	
DUNSTON, JENNIFER ANN	
ART UNIT	PAPER NUMBER
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.**	**Applicant(s)**
	09/761,893	HUNG ET AL.
	Examiner	**Art Unit**
	Jennifer Dunston	1636

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 19 December 2011 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5. ☐ Applicant's reply has overcome the following rejection(s): _____.

6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1,4,6,9-11,34,35 and 38*.
   Claim(s) withdrawn from consideration: *12-20 and 43-45*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.

12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____

13. ☒ Other: See Continuation Sheet.

/Jennifer Dunston/
Primary Examiner
Art Unit: 1636

Continuation of 11. does NOT place the application in condition for allowance because: Claims 1, 4, 6, 9, 11, 34, 35 and 38 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Caplan et al (US Patent No. 5,811,094) in view of Prockop et al (US Patent No. 7,374,937 B1) and Matsui et al (US Patent No. 4,871,674) for the reasons of record.
Applicant's arguments filed 12/19/2011 have been fully considered but they are not persuasive.
The response asserts that one of ordinary skill in the art would not have recognized that the results of the combination of Caplan, Matsui et al and Prockop et al were predictable. The response asserts that there is no finding to support the combination would improve the culture efficiency. Specifically, the response points to column 1, lines 37-39 of US Patent No. 5,652,142 to Barker et al, which states, "In the use of these cell culture inserts, gases may not be exchanged sufficiently because the area between the side-wall of the insert and the culture plate is too small." The response also points to Prockop et al (US Patent No. 7,374,937) at column 5, lines 21-28, which state, "However, prior art methods for isolating MSCs and inducing their proliferation have practical limitations, including the extent of population expansion that can be achieved using prior art methods. There remains a critical need for methods of reliably inducing significant proliferation of MSCs in culture without inducing differentiation of the MSCs as they proliferate."
These arguments are not found persuasive. Barker et al teaches that the cell culture inserts and devices described in US Patent No. 4,871,674 are conventional cell culture inserts and devices. Thus, they are generally used in the art, and the use of such inserts and devices would not have been unpredictable. Applicant has not provided evidence that the presently claimed invention requires a larger area between the side-wall of the insert and the culture plate, and the claims do not require a particular distance between the upper plate with pores and a wall of the culture device containing the upper plate. Furthermore, the statement made by Prockop et al at column 5, lines 21-28, does not provide evidence that it would have been unpredictable to combine the teachings of Caplan et al, Prockop et al, and Matsui et al. The complete passage cited by Applicant ends with "The present invention satisfies this need." See column 5, lines 27-28. Thus, the difficulties noted by Prockop et al were overcome by the disclosed invention.
The response asserts that the application has also demonstrated that "In one preferred embodiment of the present invention, the isolated MSCs proliferate without differentiation and reach confluence even after 12 passages. The cell populations having greater than 98% homogenous MSCs are obtained in accordance with the method of the present invention." Paragraph [0031] of the present application.
The response asserts that this evidence demonstrated that the results of the claimed invention were unexpected.
This argument is not found persuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., confluence after 12 passages) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Furthermore, Caplan et al (US Patent No. 5,811,094) teach "Compositions having greater than 95%, usually greater than 98% of human mesenchymal stem cells can be achieved using the previously described technique for isolation, purification and culture expansion of MSCs" (column 6, lines 29-32), where the previously described technique includes isolation and purification of human mesenchymal stem cells from tissue, such as bone marrow, by their selective attachment, termed "adherence" to substrates when cultured in a specific medium (column 6, lines 13-28). Thus, it is not unexpected that mesenchymal stem cells can be purified from bone marrow aspirate by culturing the cells on a plastic culture insert to which the mesenchymal stem cells adhere, and changing the medium to remove non-adherent cells.
The response asserts that it was not possible to combine the teachings of the reference, because in the real world, US Patent No. 7,374,937 was not disclosed until May 20, 2008.
This argument is not found persuasive. The effective date of a U.S. patent, U.S. patent application publication, or international application publication under PCT Article 21(2) is the earlier of its publication date or date that it is effective as a reference under 35 U.S.C. 102(e). The effective date of US Patent No. 7,374,937 is March 14, 2000, which is the filing date of Provisional Application No. 60/189,109. US Patent No. 7,374,937 is properly applied as art under 35 U.S.C. 103 based on the effective filing date of March 14, 2000.
For these reasons and the reasons of record, the rejection is maintained.
Claim 10 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Caplan et al (US Patent No. 5,811,094) in view of Prockop et al (US Patent No. 7,374,937 B1) and Matsui et al (US Patent No. 4,871,674), and further in view of Pittenger et al (1999).
Applicant's arguments filed 12/19/2011 have been fully considered but they are not persuasive.
Applicant does not separately argue this rejection. The arguments presented regarding the combined teachings of Caplan et al, Prockop et al, and Pittenger et al are not persuasive for the reasons set forth above.
For these reasons and the reasons of record, the rejection is maintained.
Claims 1, 4, 6, 9, 11, 34, 35 and 38 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Caplan et al (US Patent No. 5,811,094) in view of Burkitt et al (1993), and Mussi et al (US Patent No. 5,409,829).
Applicant's arguments filed 12/19/2011 have been fully considered but they are not persuasive.
The response notes that Caplan et al state that "As a whole, bone marrow is a complex tissue comprised of hematopoietic stem cells, red and white blood cells and their precursors, mesenchymal stem cells, stromal cells and their precursors, and a group of cells including fibroblasts, reticulocytes, adipocytes, and endothelial cells which form a connective tissue network called 'stroma'." Column 7, lines 12-16). The response notes that a red blood cell is only one of the components in marrow. The response asserts that there was no finding in the 12 years from the date Caplan's patent issued to support the modification.
This argument is not found persuasive. Because bone marrow is composed of many different types of cells, Caplan et al developed a process for isolating and purifying human mesenchymal stem cells (e.g., column 7, lines 37-50). Further, Caplan et al teach "Compositions having greater than 95%, usually greater than 98% of human mesenchymal stem cells can b3e achieved using the previously described technique for isolation, purification and culture expansion of MSCs" (column 6, lines 29-32), where the previously described technique includes isolation and purification of human mesenchymal stem cells from tissue, such as bone marrow, by their selective attachment, termed "adherence" to substrates when cultured in a specific medium (column 6, lines 13-28). Combining the teachings of the references would result in the predictable removal of cells other than mesenchymal stem cells.
The response asserts that the difficulties with Matuis' device also teach away from the modification.

This argument is not found persuasive. The rejection does not rely upon the teachings of Matsui, and Matsui's devices were conventionally used in the art based on the art cited by Applicant.
For these reasons and the reasons of record, the rejection is maintained.
Claim 10 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Caplan et al (US Patent No. 5,811,094) in view of Burkitt et al (1993), and Mussi et al (US Patent No. 5,409,829), and further in view of Pittenger et al (1999).
Applicant's arguments filed 12/19/2011 have been fully considered but they are not persuasive.
Applicant does not separately argue this rejection. The arguments presented regarding the combined teachings of Caplan et al, Burkitt et al, and Mussi et al are not persuasive for the reasons set forth above.
For these reasons and the reasons of record, the rejection is maintained.
Claims 1, 4, 6, 9, 11, 34, 35 and 38 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Caplan et al (US Patent No. 5,811,094) in view of Guirguis (US Patent No. 5,077,012) and Matsui et al (US Patent No. 4,871,674).
Applicant's arguments filed 12/19/2011 have been fully considered but they are not persuasive.
The response asserts that Guirguis disclosed "An apparatus for collecting biological fluids and holding samples taken from a biological fluid for qualitative and quantitative testing (Abstract). The response asserts that no finding supports that one of ordinary skill in the art of stem cells would refer to the disclosure of Guirguis, which is "an apparatus for detecting disease markers both for screening as well as for a reference laboratory setting." (Column 1, lines 15-17). The response asserts that the two fields are different.
In response to applicant's argument that Guirguis is nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See In re Oetiker, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, Caplan et al teach the removal of red blood cells from bone marrow aspirate (body fluid) for the purpose of providing purified mesenchymal stem cells (column 8, lines 20-44; column 11, lines 35-62). Guirguis teaches the removal of red blood cells from a body fluid using a membrane with a smooth flat surface, which is ideal for the collection of atypical cells from all types of body fluids (e.g., column 3, lines 37-45; column 4). Guirguis teaches that the membrane has a preferred pore size of 2 microns or less (e.g., column 4, lines 14-19). Guirguis teaches that the advantage of using a polycarbonate membrane is the minimum clogging by red blood cells and protein, well preserved cellular morphology with a high recovery rate, and excellent surface capture due to the pore structure and porosity (e.g., column 4, lines 43-64). Thus, one would have recognized that the membrane of Guirguis could be used to remove blood cells from the nucleated cells of the bone marrow aspirate of Caplan et al. The references are both in the same field of endeavor related to cell separation.
The response asserts that the difficulty of using Matsui's device would teach away from the modification. Specifically, the response points to column 1, lines 37-39 of US Patent No. 5,652,142 to Barker et al, which states, "In the use of these cell culture inserts, gases may not be exchanged sufficiently because the area between the side-wall of the insert and the culture plate is too small."
This argument is not found persuasive. Barker et al teaches that the cell culture inserts and devices described in US Patent No. 4,871,674 are conventional cell culture inserts and devices. Thus, they are generally used in the art, and the use of such inserts and devices would not have been unpredictable. Applicant has not provided evidence that the presently claimed invention requires a larger area between the side-wall of the insert and the culture plate, and the claims do not require a particular distance between the upper plate with pores and a wall of the culture device containing the upper plate. Matsui et al does not criticize or discredit the use of a porous polycarbonate membrane to remove red blood cells.
The response asserts that the rejection has been overcome by a showing of unexpected results in the specification. The response indicates that the unexpected results are claimed in claims 43-45 and include culture to confluence even after 12 passages. The response points to the post-filing art as indicating that proliferation of stem cells stops or becomes extremely slow around the 15th generation.
These arguments are not found persuasive. Claims 43-45 are withdrawn from consideration as being drawn to a non-elected invention. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., confluence after 12 passages) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Furthermore, Caplan et al (US Patent No. 5,811,094) teach "Compositions having greater than 95%, usually greater than 98% of human mesenchymal stem cells can be achieved using the previously described technique for isolation, purification and culture expansion of MSCs" (column 6, lines 29-32), where the previously described technique includes isolation and purification of human mesenchymal stem cells from tissue, such as bone marrow, by their selective attachment, termed "adherence" to substrates when cultured in a specific medium (column 6, lines 13-28). Thus, it is not unexpected that mesenchymal stem cells can be purified from bone marrow aspirate by culturing the cells on a plastic culture insert to which the mesenchymal stem cells adhere, and changing the medium to remove non-adherent cells.
For these reasons and the reasons of record, the rejection is maintained.
Claim 10 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Caplan et al (US Patent No. 5,811,094) in view of Guirguis, and Matsui et al, and further in view of Pittenger (1999).
Applicant's arguments filed 12/19/2011 have been fully considered but they are not persuasive.
Applicant does not separately argue this rejection. The arguments presented regarding the combined teachings of Caplan et al, Guirguis, and Matsui et al are not persuasive for the reasons set forth above.
For these reasons and the reasons of record, the rejection is maintained.

Continuation of 13. Other: Claims 43-45 should have been provided with the status identifier "Withdrawn." However, the amendment has been entered in the interest of compact prosecution.